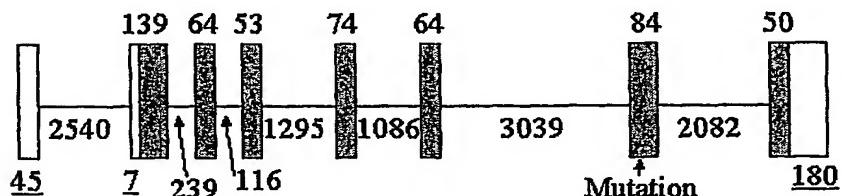


**Figure 1A.**

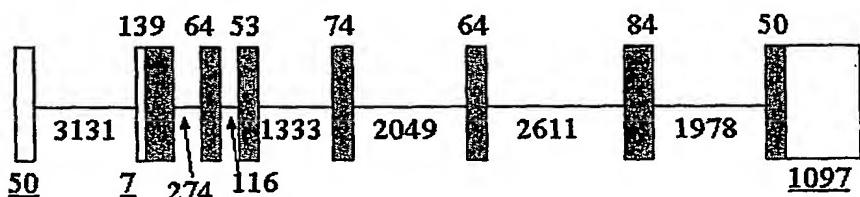
Mouse ID	Mouse Gene Description	Chrom	Mouse ID	Human Gene Description	Chrom	Human ID	
092324	NEPHROG OF ATONAL 3	12	28041629	096RJ6	NEPHROG OF ATONAL 3	7	16829031
NH_011658	TWIST RELATED PROTEIN (H-TWIST)	12	28071270	TWIST	TWIST RELATED PROTEIN (H-TWIST)	7	16800882
NH_024124	HISTONE DEACETYLASE 9 (HD9) (HD7B)	12	28486280	NH_014707	HISTONE DEACETYLASE 9 (HD9) (HD7B) (HD7)	7	16179912
NH_013464	AH RECEPTOR PRECURSOR (AHR)	12	29623298	AHR	AH RECEPTOR (ARYL HYDROCARBON RECEPTOR) (AHR)	7	16982797
EC023499	SIMILAR TO ANTERIOR GRADIENT PROTEIN 3	12	30054072	Q8TD06	ANTERIOR GRADIENT PROTEIN 3	7	16543709
U68312	ANTERIOR GRADIENT 3 (HOMEODOMAIN-CONTAINING PROTEIN)	12	30112538	NCBI274	ANTERIOR GRADIENT 3 (HOMEODOMAIN-CONTAINING PROTEIN)	7	16475002
HDX2	HOUSE HOMEBOX PROTEIN HOX-2	12	31233665	HOXA2	HOMEBOX PROTEIN HOX-2	7	15295209
NM_007960	ETS1 PROTEIN (ETS TRANSLOCATION VARIANT 1)	12	32910756	ETV1	ETS TRANSLOCATION VARIANT 1 (ETS1 PROTEIN)	7	13579610
NM_007487	ADP-RIBOSYLATION FACTOR-LIKE PROTEIN 4	12	34165437	ARL4	ADP-RIBOSYLATION FACTOR-LIKE PROTEIN 4	7	12370905
NM_009132	ADSVERIN (SCINDERIN) (GELSOLIN-LIKE PROTEIN)	12	34169389	Q96FT2	ADSVERIN (SCINDERIN)	7	12254575

**Figure 1B.**

Mouse Agr 2 (Chr.12: 30,11 Mb)



Human Agr 2 (Chr.7: 16,48 Mb)



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**Figure 2.****BLAST 2 Sequences**

(<http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html>)

Sequence 1: mouse AGR2 (WT); SEQ ID No:3  
Sequence 2: human AGR2 (WT); SEQ ID No:4

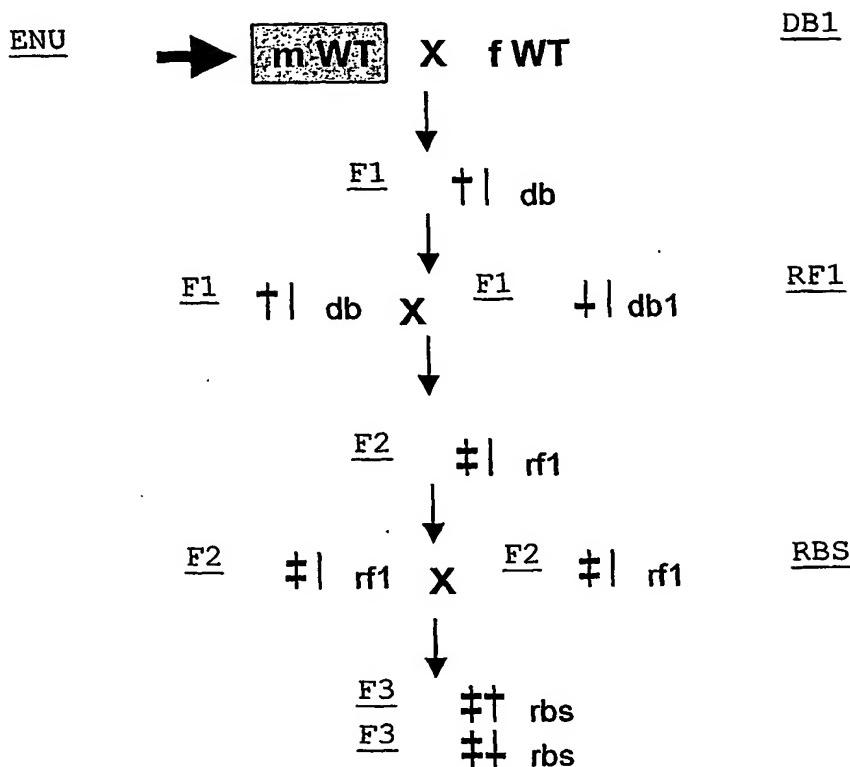
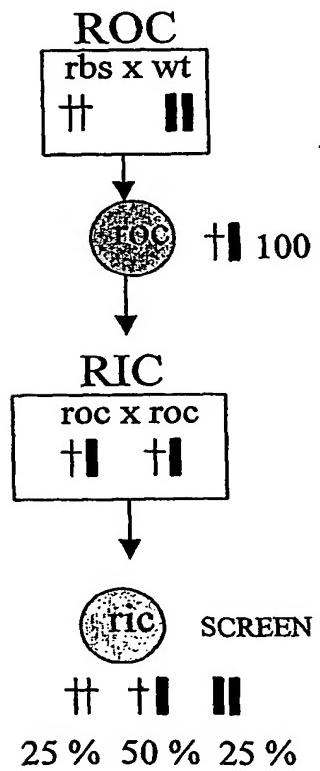
NOTE: The statistics (bitscore and expect value) is calculated based on the size of nr database.

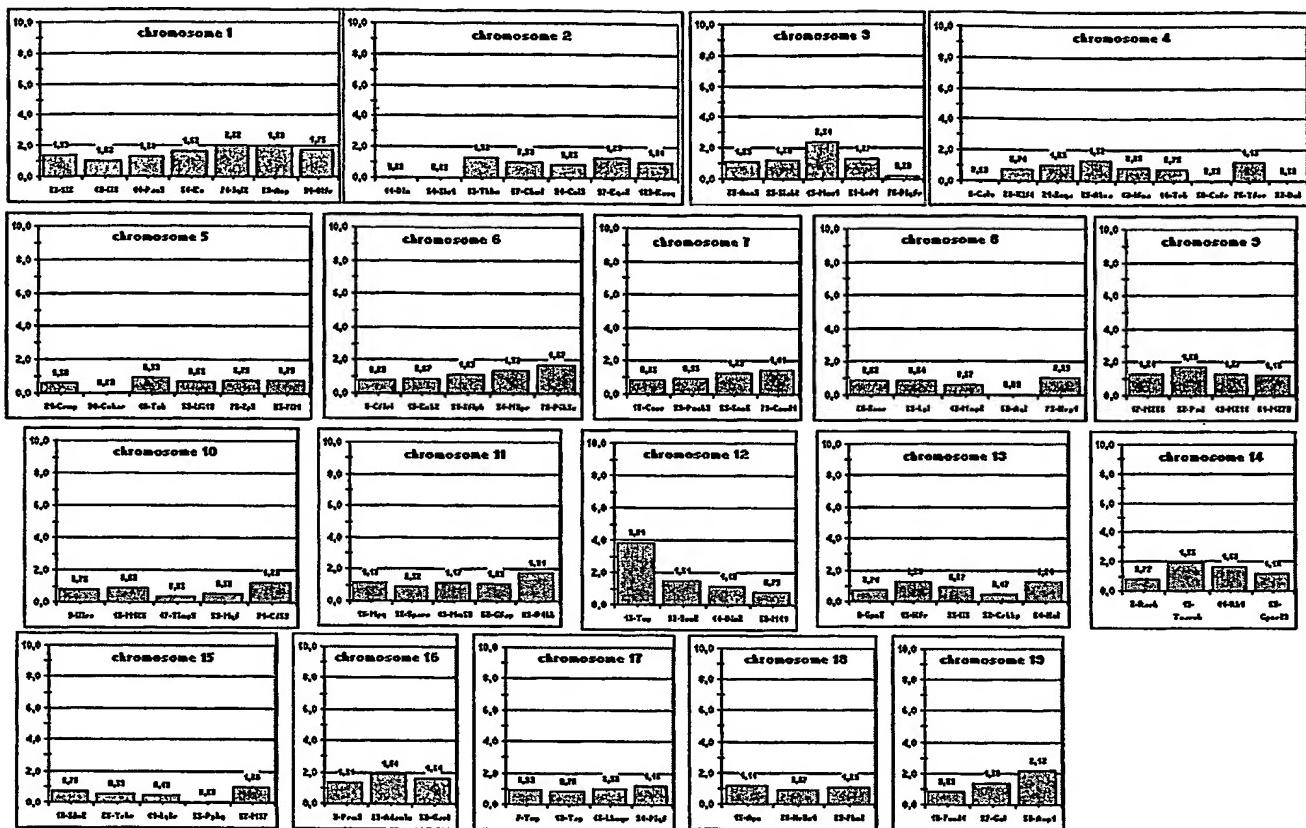
Score = 323 bits (828), Expect = 4e-88  
Identities = 160/175 (91%), Positives = 168/175 (95%)

Query: 1 MEKFSVSAI<sub>LLL</sub>VAISGTLAKDTTVKSGAKKD<sub>P</sub>KDSRP<sub>K</sub>L<sub>P</sub>QTL<sub>S</sub>RGWGDQLIWTQTYEE 60  
MEK VSA LLLVA+S TLA+DTTVK GAKKD KDSRP<sub>K</sub>L<sub>P</sub>QTL<sub>S</sub>RGWGDQLIWTQTYEE  
Sbjct: 1 MEKIPVSAF<sub>LLL</sub>VALSYTLARDTTVKPGAK<sub>K</sub>D<sub>T</sub>KDSRP<sub>K</sub>L<sub>P</sub>QTL<sub>S</sub>RGWGDQLIWTQTYEE 60  
Query: 61 ALYRSKTSNRPLMVI<sub>HH</sub>LDEC<sub>P</sub>H<sub>S</sub>QALKVFAEHKEI<sub>Q</sub>KLAEQFVLLNLVYETTDKHLSP 120  
ALY+SKTSN+PLM+I<sub>HH</sub>LDEC<sub>P</sub>H<sub>S</sub>QALKVFAE+KEI<sub>Q</sub>KLAEQFVLLNLVYETTDKHLSP  
Sbjct: 61 ALYKSKTSNKPLMII<sub>HH</sub>LDEC<sub>P</sub>H<sub>S</sub>QALKVFAENKEI<sub>Q</sub>KLAEQFVLLNLVYETTDKHLSP 120  
Query: 121 DGQYVPRIVFVDPSLT<sub>V</sub>RADITGRYSNR<sub>L</sub>YAYEP<sub>S</sub>DTALLYDNMKKALKLLKTEL 175  
DGQYVPRI+FVDPSLT<sub>V</sub>RADITGRYSNR<sub>L</sub>YAYEP+DTALL DNMKKALKLLKTEL  
Sbjct: 121 DGQYVPRIMFVDPSLT<sub>V</sub>RADITGRYSNR<sub>L</sub>YAYEPADTALLDNMKKALKLLKTEL 175

**Figure 3.**

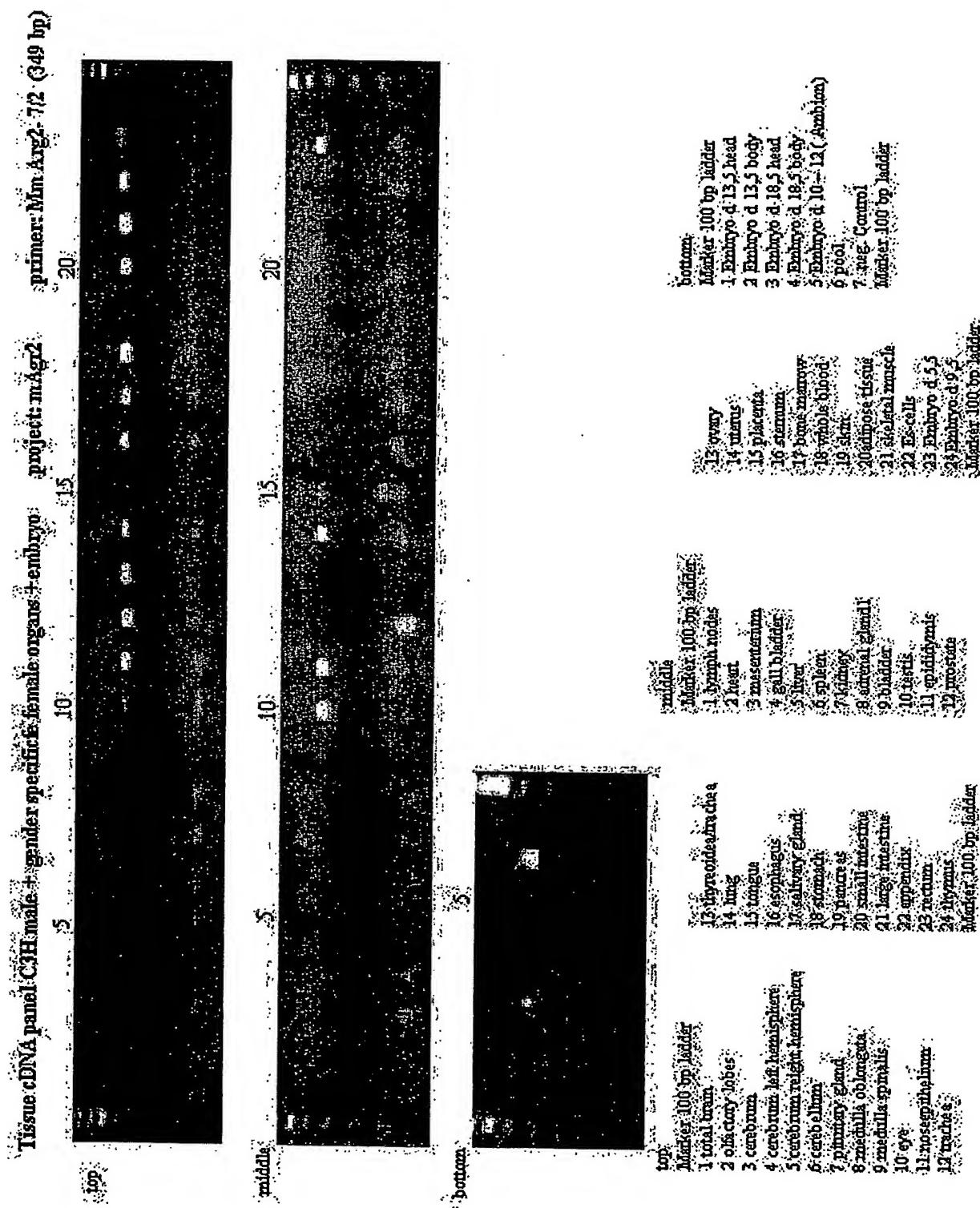
**Breeding-Scheeme:**  
**A) F3 production**

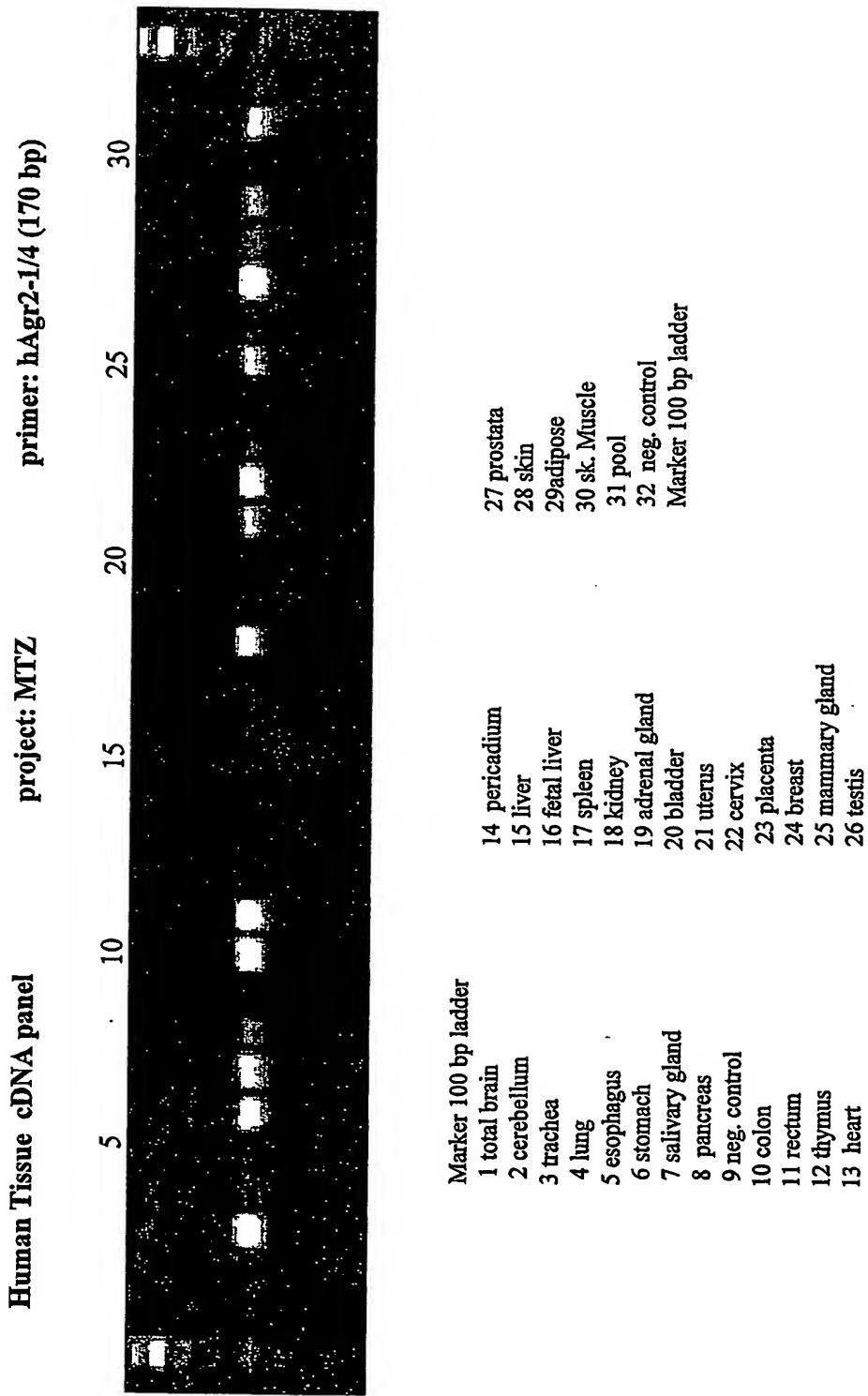
**B) Outcross**

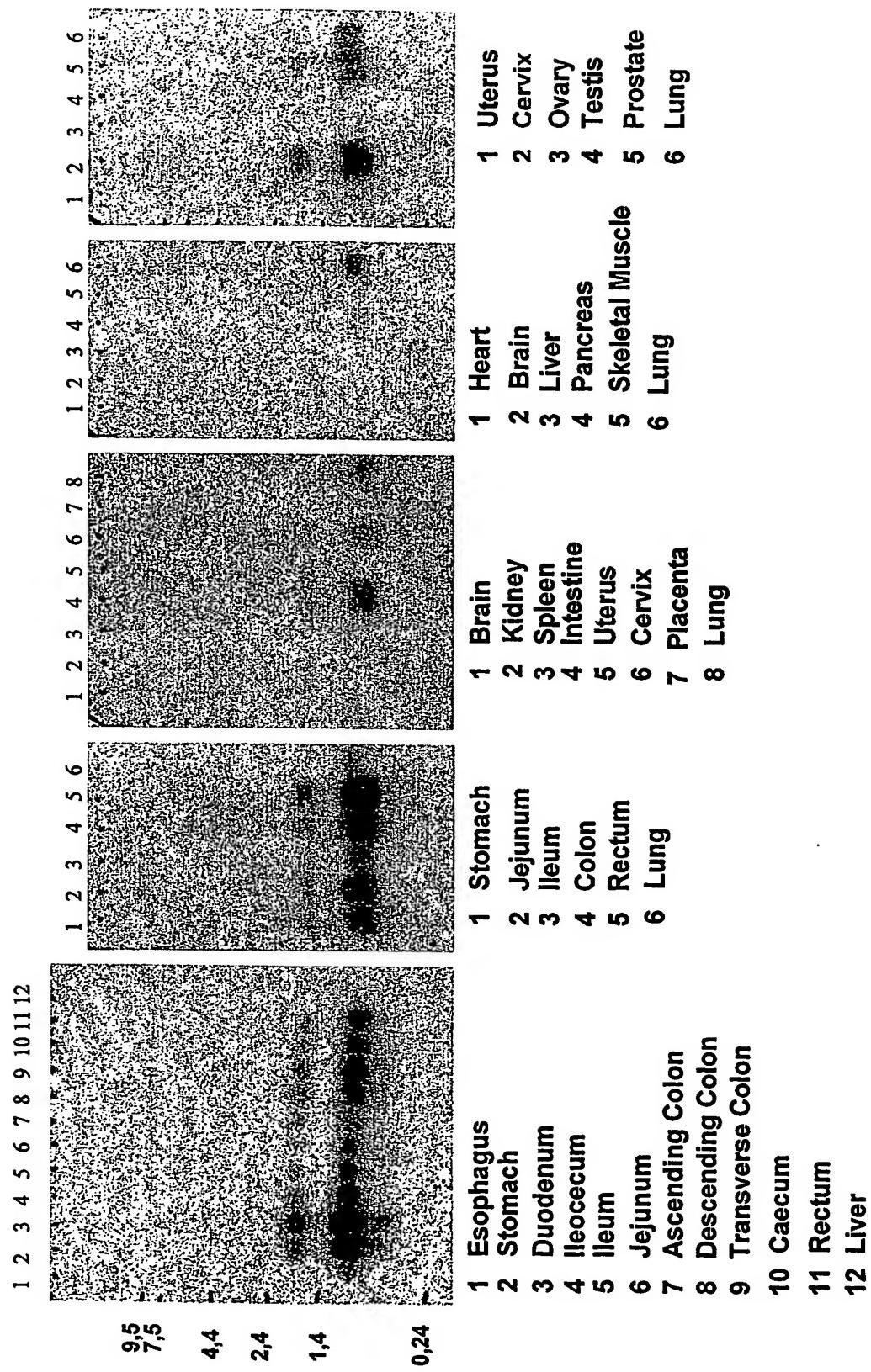
**Figure 4.**

**Figure 5.****Haplotypes Scheme**

	appr. cM Marker	appr. Mb			
6	D12Mit12	18,7	c	c	
7	Idb2	19,1	c	c	
10	D12Mit171	23,4	c	c	c
8	Slc26a3	25,5	c	c	c
14	D12Mit221	40,3	c	c	c
18	D12Mit64	44,8			c
19	D12Mit110	46,3			c
25	D12Mit285	49,1	b		c
			SEX MOUSE	m #899	f #799
					m #764

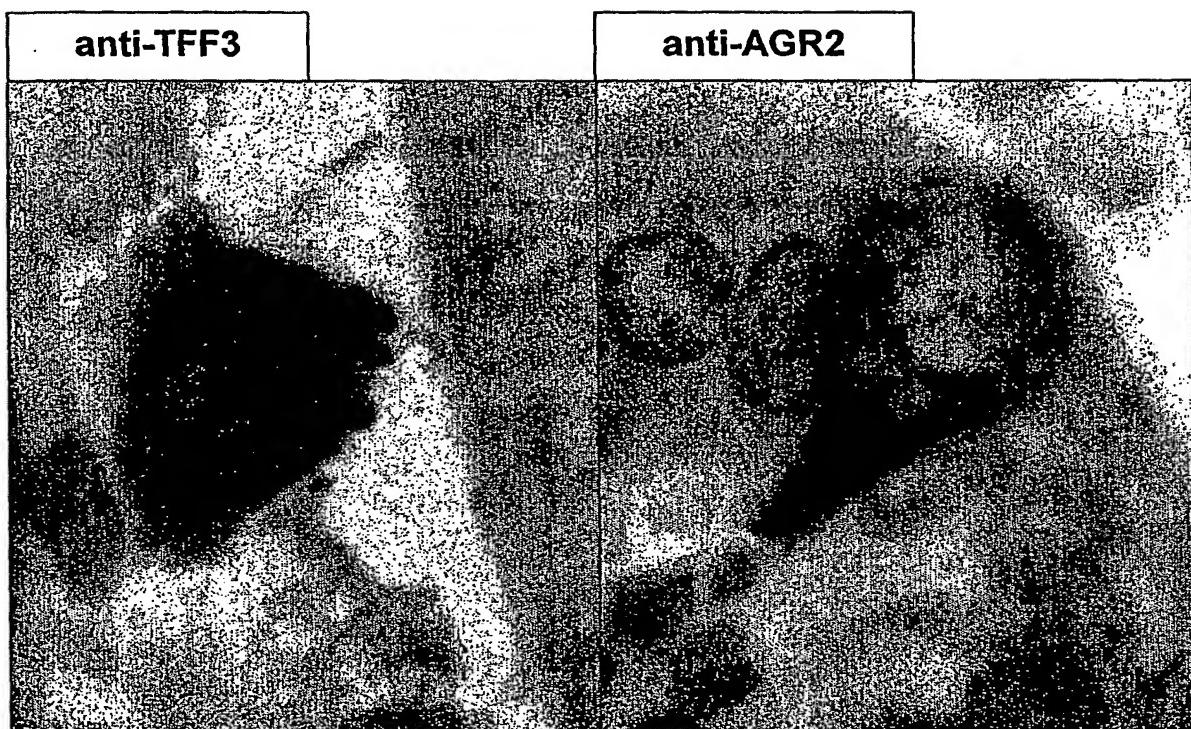
**Figure 6**

**Figure 7.**

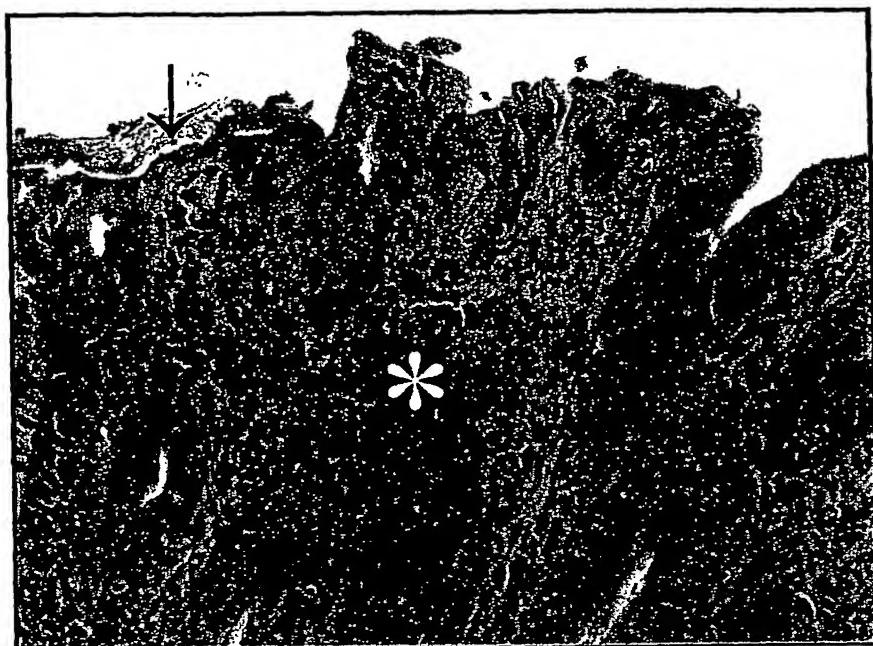
**Figure 8.**

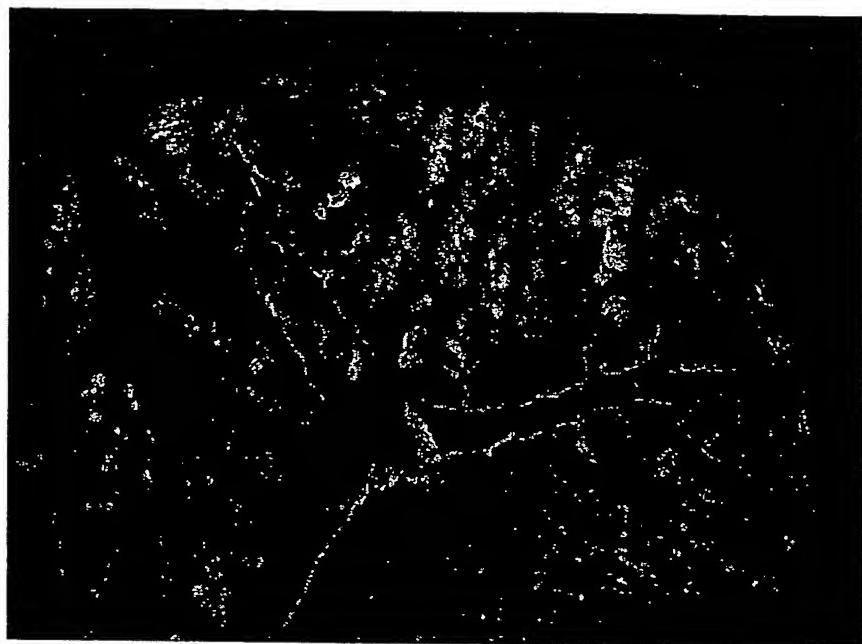
**Figure 9.**

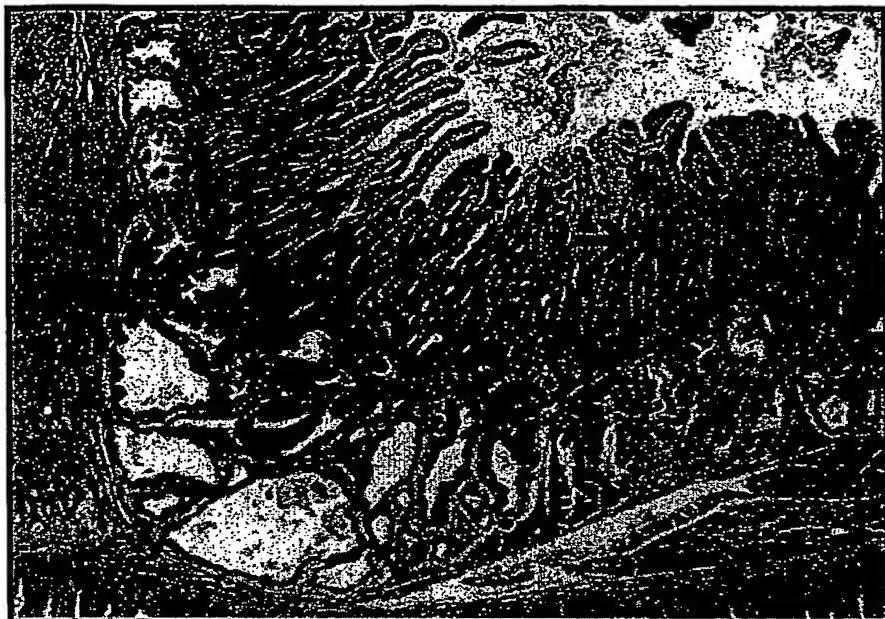
mouse number	genotype	thriving	chronic deficit	diarrhea
1	mut	yes	yes	
2	mut	yes	yes	
3	mut	yes	yes	
4	mut	yes	yes	
5	mut	yes	yes	
6	hz	no	no	
7	hz	no	no	
8	hz	no	no	
9	hz	no	no	
10	hz	no	no	
11	hz	no	no	
12	hz	no	no	
13	hz	no	no	
14	hz	no	no	
15	hz	no	no	
16	hz	no	no	
17	hz	no	no	
18	hz	no	no	
19	wt	no	no	
20	wt	no	no	
21	wt	no	no	
22	wt	no	no	
23	wt	no	no	
24	wt	no	no	
25	wt	no	no	

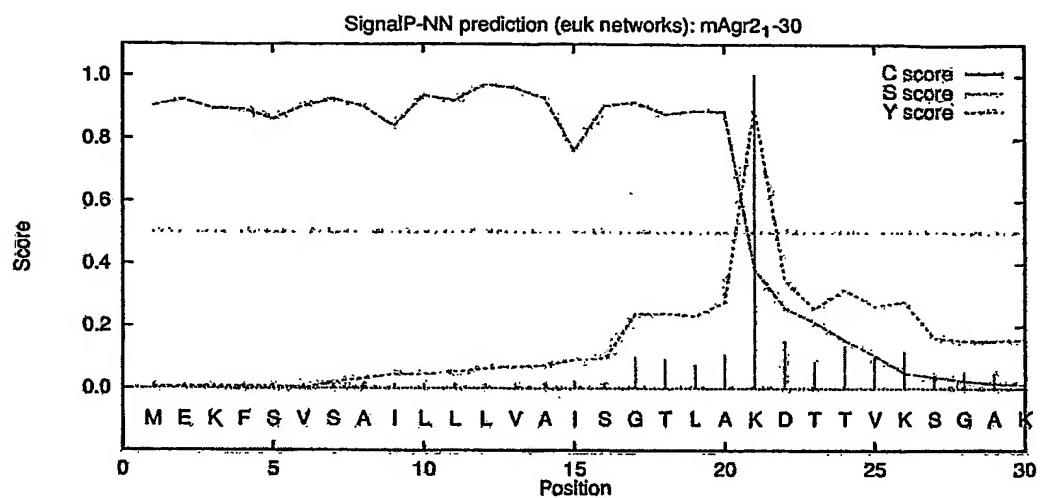
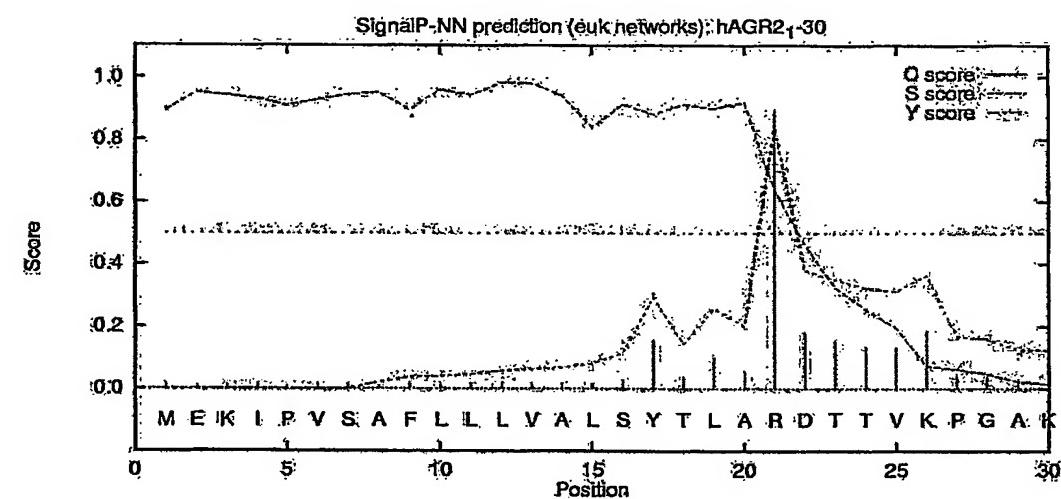
**Figure 10.**

**Figure 11.****Colon (wild type mouse)****Colon (affected mouse)**

**Figure 12.****Colon (affected mouse)**

**Figure 13.****Colon (wild type mouse)****Colon (affected mouse)**

**Figure 14.****Brunner's gland (wild type mouse)****Brunner's gland (affected mouse)**

**Figure 15A.****Figure 15B.**

**Figure 16.**

Software used:

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988),  
Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22),  
10881-10890]
- BOXSHADE 3.21 via [http://www.ch.embnet.org/software/BOX\\_form.html](http://www.ch.embnet.org/software/BOX_form.html)

Mm: *Mus musculus*; NP\_035913Hs: *Homo sapiens*; NP\_006399Rn: *Rattus norvegicus*; derived by Genewise on AC126809

Mm	1	MEKFSVSAI <del>L</del> LLVAISGTLAKDTTVKSGAKKDPKDSRPKLQ <del>T</del> LSRGWG <del>D</del> QLIWTQTYEE
Rn	1	MEKFSVSAI <del>L</del> LLVAISGTLAKDTTVKSG <del>S</del> KKDPKDSRPKLQ <del>T</del> LSRGWG <del>D</del> QLIWTQTYEE
Hs	1	MEK <del>I</del> PVSA <del>E</del> LLVAISGTLAKDTTVKPGAKKD <del>T</del> KDSRPKLQ <del>T</del> LSRGWG <del>D</del> QLIWTQTYEE
<b>Consensus</b>	<b>1</b>	<b>MEKFSVSAI<del>L</del>LLVAISGTLAKDTTVKSGAKKDPKDSRPKLQ<del>T</del>LSRGWG<del>D</del>QLIWTQTYEE</b>
Mm	61	ALY <del>E</del> SKTSNRPLMVI <del>H</del> HDEC <del>P</del> HSQLKKVFAE <del>H</del> KEI <del>Q</del> KLAEQFV <del>L</del> NLVYETTDKHLSP
Rn	61	ALYKS <del>K</del> TSNRPLMVI <del>H</del> HDEC <del>P</del> HSQLKKVFAENKEI <del>Q</del> KLAEQFV <del>L</del> NL <del>E</del> ETTDKHLSP
Hs	61	ALYKS <del>K</del> TSN <del>K</del> PLM <del>I</del> <del>H</del> HDEC <del>P</del> HSQLKKVFAENKEI <del>Q</del> KLAEQFV <del>L</del> NLVYETTDKHLSP
<b>Consensus</b>	<b>61</b>	<b>ALYKS<del>K</del>TSNRPLM<del>I</del><del>H</del>HDEC<del>P</del>HSQLKKVFAENKEI<del>Q</del>KLAEQFV<del>L</del>NL<del>E</del>ETTDKHLSP</b>
 <b>VMTZ (VVE)</b>		
Mm	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLYDNMKKALKLLKTEL
Rn	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLHDNMKKALKLLKTEL
Hs	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALLLDNMKKALKLLKTEL
<b>Consensus</b>	<b>119</b>	<b>DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPSDTALL.DNMKKALKLLKTEL</b>

Percentage of identical and similar amino acids: 95.4%  
 Percentage of identical amino acids: 90.8%

**Figure 17.**

#### **Software used:**

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988), Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22), 10881-10890]
  - BOXSHADE 3.21 via [http://www.ch.embnet.org/software/BOX\\_form.html](http://www.ch.embnet.org/software/BOX_form.html)

Mm: *Mus musculus*; NP\_035913  
Hs: *Homo sapiens*; NP\_006399  
Rn: *Rattus norvegicus*; derived by Genewise on AC126809  
Xl: *Xenopus laevis*; AAL26844

Mm	1 MEKFSVSAI <del>L</del> LLVAISGTLAKDTTVKSGAKKDEKDSRPKLQTL <del>S</del> RGWGDQLIWTQTYEE
Rn	1 MEKFSVSAI <del>L</del> LLVAISGTLAKDTTVKSGSKKDEKDSRPKLQTL <del>S</del> RGWGDQLIWTQTYEE
Hs	1 MEKIPVS <del>A</del> FLLLV <del>A</del> LSYTLA <del>D</del> TTVKPGAKKD <del>T</del> KDSRPKLQTL <del>S</del> RGWGDQLIWTQTYEE
X1	1 MET <del>V</del> LKS <del>I</del> FELLVATSETLAKE <del>E</del> ..... <del>E</del> KPOTL <del>S</del> RGWGD <del>I</del> LEW <del>V</del> QTYEE
Consensus	1 MEK..VSAF <del>L</del> LLVA. <del>S.</del> TLAK#TTVK.GAKKD.KDSRPKLQTL <del>S</del> RGWGD#LIWTQTYEE

Mm	61	ALY <b>E</b> SKTSNRP <b>L</b> MMI <b>H</b> HLDEC <b>P</b> HSQALKKVFAE <b>H</b> KE <b>I</b> QKLA <b>E</b> QFVLLNLV <b>Y</b> ETTD <b>K</b> HL <b>F</b>
Rn	61	ALY <b>K</b> SKTSNRP <b>L</b> MMI <b>H</b> HLDEC <b>P</b> HSQALKKVFAE <b>N</b> KE <b>I</b> QKLA <b>E</b> QFVLLNL <b>Y</b> ETTD <b>K</b> HL <b>F</b>
Hs	61	ALY <b>K</b> SKTSNKP <b>L</b> MMI <b>H</b> HLDEC <b>P</b> HSQALKKVFAE <b>N</b> KE <b>I</b> QKLA <b>E</b> QFVLLNLV <b>Y</b> ETTD <b>K</b> HL <b>F</b>
X1	45	<b>G</b> LE <b>K</b> A <b>K</b> SENKP <b>L</b> LLIN <b>H</b> R <b>M</b> DC <b>P</b> HSQALK <b>K</b> A <b>F</b> A <b>E</b> <b>R</b> O <b>G</b> I <b>Q</b> KLA <b>E</b> <b>E</b> F <b>T</b> LL <b>N</b> V <b>Y</b> <b>L</b> PTDK <b>N</b> <b>L</b> <b>O</b> <b>L</b>
Consensus	53	AL <b>K</b> SKTSNKP <b>L</b> \$.I <b>H</b> HL <b>#</b> <b>#</b> <b>C</b> PHS <b>Q</b> ALK <b>K</b> V <b>F</b> A <b>E</b> N <b>K</b> E <b>I</b> Q <b>K</b> LA <b>E</b> <b>E</b> F <b>T</b> LL <b>N</b> L <b>Y</b> <b>L</b> PTDK <b>N</b> <b>L</b> <b>O</b> <b>L</b>

		<b>VMTZ (VVE)</b>
Mm	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEP <del>S</del> D <sup>T</sup> ALLYDNMKKALKLLKTEL
Rn	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEP <del>S</del> D <sup>T</sup> ALLHDNMKKALKLLKTEL
Hs	121	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPADTALLLDNMKKALKLLKTEL
X1	105	DGQYVPRIVFVDPSLTVRADITPGKYSNH <del>O</del> TYEPADIDHLEENMKKALVLLKTEL
Consensus	104	DGQYVPRIVFVDPSLTVRADITGRYSNRLYAYEPADTALLL <del>#</del> NMKKALKLLKTEL

Percentage of identical and similar amino acids: 82%  
Percentage of identical amino acids: 67%

## Figure 18.

Software used:

- MultAlin via <http://prodes.toulouse.inra.fr/multalin/multalin.html> [Corpet. F. (1988), Multiple sequence alignment with hierarchical clustering, Nucl. Acids Res., 16 (22), 10881-10890]
- BOXSHADE 3.21 via [http://www.ch.embnet.org/software/BOX\\_form.html](http://www.ch.embnet.org/software/BOX_form.html)

Mm: *Mus musculus*; NP\_035913  
 Hs: *Homo sapiens*; NP\_006399  
 Rn: *Rattus norvegicus*; derived by Genewise on AC126809  
 Xl: *Xenopus laevis*; AAL26844  
 Ce: *Caenorhabditis elegans*; NP\_496599

Mm	1 MEKESVSAI <del>LLL</del> VALISGT <del>LA</del> KDTTVKSGAKKDEKDSRPKLPQTL <del>SRG</del> WG <del>D</del> QLIW <del>T</del> QTYEE
Rn	1 MEKESVSAI <del>LLL</del> VALISGT <del>LA</del> KDTTVKSGSKDPEKDSRPKLPQTL <del>SRG</del> WG <del>D</del> QLIW <del>T</del> QTYEE
Hs	1 MEKIPVSAF <del>LL</del> LVALS <del>Y</del> T <del>LA</del> E <del>D</del> T <del>V</del> KPGAKKDTKDSRPKLPQTL <del>SRG</del> WG <del>D</del> QLIW <del>T</del> QTYEE
Xl	1 METVLKSLF <del>LL</del> LVALT <del>S</del> FTLAKE. .... .RKPQTL <del>SRG</del> WG <del>D</del> NLEWVQTYEE
Ce	1 .... MRSLL <del>LL</del> LALVSASAYASFDK <del>E</del> KD. .... .S1QNPLAR <del>G</del> E <del>G</del> D <del>D</del> IAWVK. WED
<b>Consensus</b>	1 MEK..VSA.LLLVA.S.TLAKDTTVK.G.KKD.KDSRPKLP#TLSRGWGD#LIWTQTYE#

Mm	61 ALYRSKTSNF <del>PLM</del> VIHH <del>L</del> DEC <del>P</del> HSQALKKVFAEH. .... KEIQKLAEQFVLLNLVY..ETTD
Rn	61 ALYKS <del>K</del> TSNF <del>PLM</del> VIHH <del>L</del> DEC <del>P</del> HSQALKKVFAEN. .... KEIQKLAEQFVLLNLVY..ETTD
Hs	61 ALYKS <del>K</del> TSN <del>KPLM</del> VIHH <del>L</del> DEC <del>P</del> HSQALKKVFAEN. .... KEIQKLAEQFVLLNLVY..ETTD
Xl	45 GLEFRK <del>K</del> SEN <del>KPLM</del> LIINHRN <del>E</del> CPHSQALKKAFAEH. .... QGIQKLAEEFELLNWVY..DPTD
Ce	45 ATET <del>E</del> LDTDKPIELLIHKSWCHACKALKKTFOQSNAKAFKKLSEH <del>F</del> V <del>E</del> VNTEDDDEEE
<b>Consensus</b>	50 ALYKS <del>K</del> TS# <del>KPLM</del> .IHH <del>L</del> DEC <del>P</del> HSQALKKVFA#. .... KEIQKLAEQF!.S <del>LN</del> LVY..#TT#

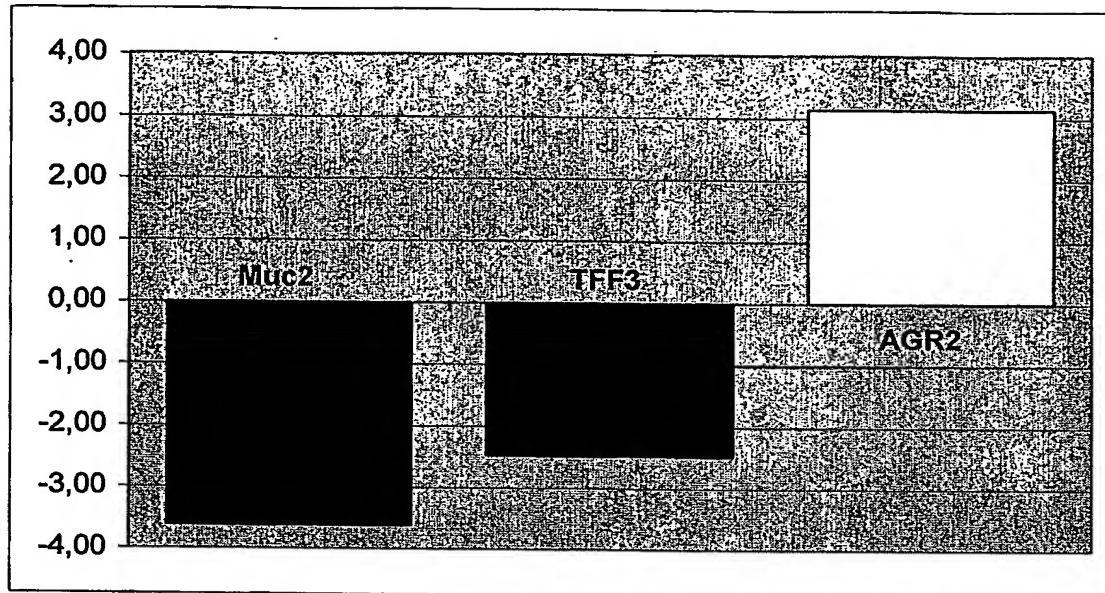
<b>▼MTZ (VVE)</b>	
Mm	116 KHLSPDGQYVPRIVFVDPSLT <del>V</del> RADITGRYSN. RLYAYEPSDTALLYDNMKKALKLLKTE
Rn	116 KHLSPDGQYVPRIVFVDPSLT <del>V</del> RADITGRYSN. RLYAYEPSDTALLHDNMKKALKLLKTE
Hs	116 KHLSPDGQYVPRIVFVDPSLT <del>V</del> RADITGRYSN. RLYAYEPSDTALLDNMKKALKLLKTE
Xl	100 KNLQLDQYVPLWVFVDPSL <del>V</del> VRADLPG <del>Y</del> SN. HOYT <del>Y</del> EPADIDHLFENMKKALVLLKTE
Ce	105 E <del>E</del> YRPDGK <del>Y</del> IPRLIFIDKNGDLLOE <del>E</del> FKNNKA <del>E</del> YKNYAYYYSSPADILNSMKDVLKHF <del>G</del> V <del>D</del>
<b>Consensus</b>	97 KHLSPDGQY!PRIVFVDPSLT <del>V</del> R#ITGRYS#. RLYAYEPSDTALL.#NMKKALKLLKT#

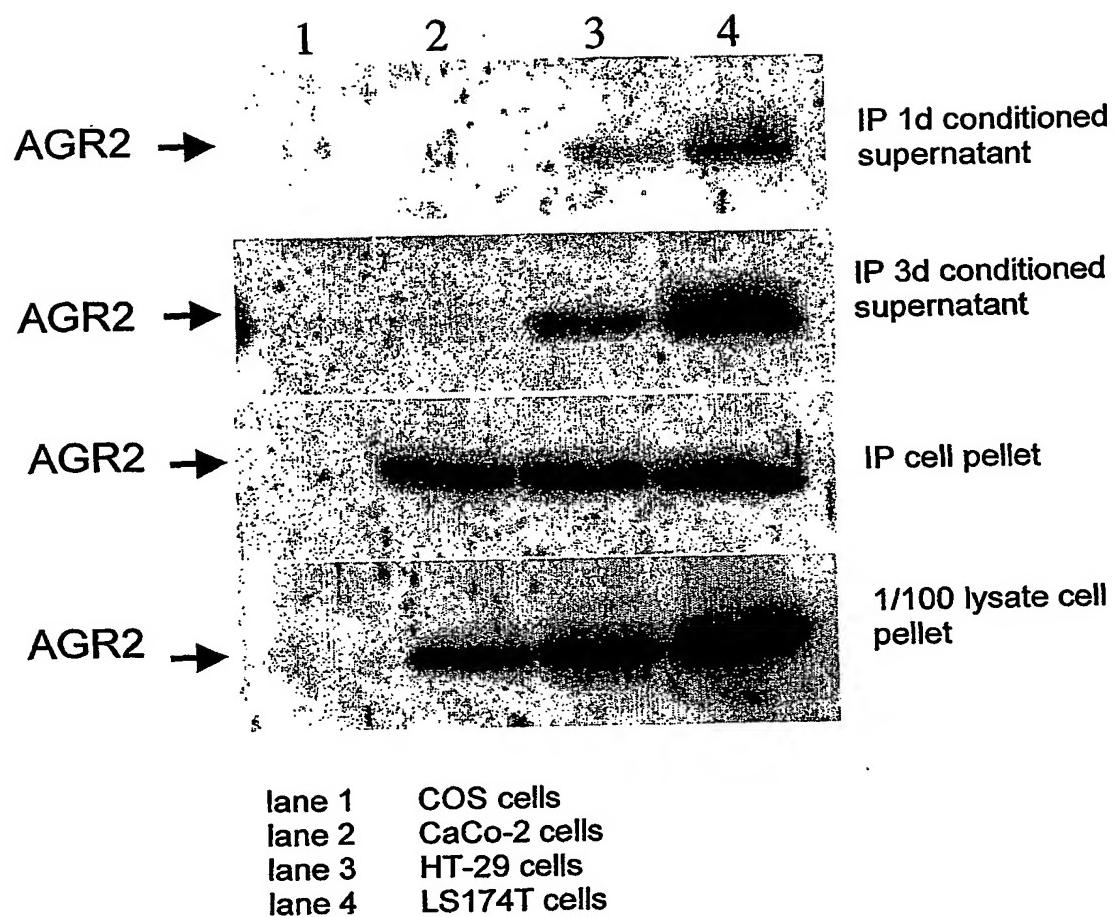
Mm	175 L. ....
Rn	175 L. ....
Hs	175 L. ....
Xl	159 L. ....
Ce	165 IPEAKRGDKLKP <del>K</del> KKPEGKKEL
<b>Consensus</b>	150 L. ....

Percentage of identical and similar amino acids: 32%  
 Percentage of identical amino acids: 46%

**Figure 19.**

mRNA regulation  
[fold change relative to  
reference marker ALAS]



**Figure 20.**

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